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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,000	03/16/2004	Thomas Nadackal Thomas	1996.01	2824

21901 7590 12/08/2011

Smith & Hopen, P.A.
Attn: General Patent Matters
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EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
12/08/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/802,000	THOMAS, THOMAS NADACKAL	
	Examiner	Art Unit	
	PHYLLIS SPIVACK	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-6 and 8-34* is/are pending in the application.

5a) Of the above claim(s) *6,8-16,18,19 and 21-34* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-5, 17, 20* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after Final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 1, 2010 has been entered.

Claims 1-6 and 8-34 are pending. Claims 6, 8-16, 18, 19 and 21-34 remain withdrawn from consideration, 37 CFR 1.142(b), as drawn to non-elected inventions. Claims 1-5, 17 and 20 remain under consideration.

In response to an Election of species Requirement, on August 15, 2011 Applicant elected aspirin as the anti-inflammatory drug. Applicant previously elected the MAO inhibitors deprenyl and propargylamine. On October 16, 2007 Applicant elected to prosecute Group I, claims, 1-5, 7, 17 and 20, in response to the Restriction Requirement set forth on September 20, 2007. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

On April 14, 2011 the following was communicated to Applicant on page 3 of the Election of Species Requirement:

In order for this election to be considered fully responsive to this requirement, the election must include:

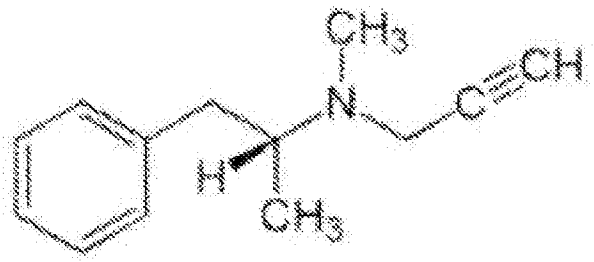
a) the name and structure of the elected species, including a depiction of the chemical linkage of an anti-inflammatory and a MAO inhibitor (presently limited to deprenyl or propargylamine) AND a depiction of the structure contemplated by the

elected specie in instant formula 1 of claim 20;

b) the location of the species within the claims or within the specification; and

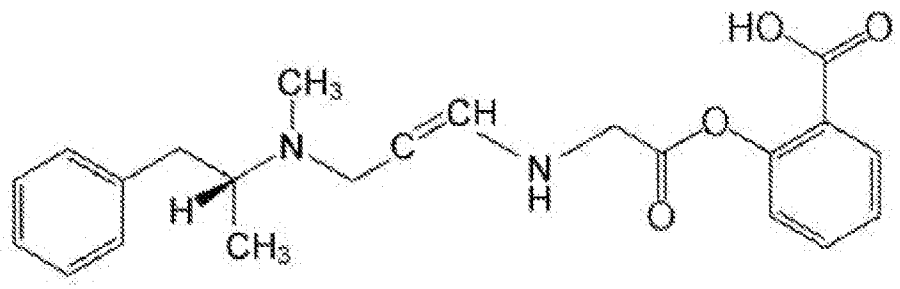
c) the claims that read on the elected species.

In response, on August 15, 2011, Applicant provided the following structures and explanation, particularly with respect to the compounds contemplated for formula I, recited in claim 20. The first compound depicts deprenyl and the second compound depicts propargylamine.



, and

Formula 1 of claim 20 is $RC{\equiv}CCH_2NH_2$. An example of a compound of formula 1 is provided as:



where it is stated a NSAID can be linked to a MAO inhibitor of the propargylamine type with formula 1 **to form an amide bond**, where R is a hydrogen, alkyl $[CH_3CH_2)_n$ and n is an integer from 1-20, aryl, alkyl aryl group or alkoxy or aryloxy group and salts thereof and other monoamine oxidase (MAO A and B) inhibitors containing a propargyl group. In cases where the MAO inhibitors do not have a free amino group available, as in the case of deprenyl, clorgyline or pargyline, a free amino group is introduced at the at the propyl carbon by arts known in the literature.

This example clearly relates to a conjugate of deprenyl and aspirin. Deprenyl does not have a free amino group. No amide bond is noted. No propyl group is depicted. No depiction of a conjugate of propargylamine and aspirin is provided.

The rejections presented or maintained in the last Office Action are withdrawn. The following objection and rejections represent the only objection and rejections presently applied to the instant claims.

The disclosure is objected to for the following informality:

Claim 23 is presently withdrawn from consideration and should be described as such.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In claim 20 the term "general" before "formula (1)" has no probative value and should be deleted.

An amide contains the functional group consisting of a carbonyl group (R-C=O) linked to a nitrogen atom. While a free amino group is present in propargylamine, it is not seen in the deprenyl structure. Because the linkage of neither deprenyl nor propargylamine is clearly provided, those compounds encompassed by formula 1, claim 20, are unclear.

Claim 17 lacks clear antecedent basis in claim 1 from which it depends. Claim 1 recites "gastrointestinal ulceration effects." Claim 17 recites "the MAO inhibitor prevents or treats the toxic side effect**s** of NSAIDS" and is broader than claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 17 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written Description Rejection.

Adequate description is provided for reducing aspirin-induced gastric lesions following the administration of l-deprenyl, the combination of aspirin + l-deprenyl and the combination aspirin-propargylamine. See Table 3, page 25. There is insufficient written description for preventing, reducing or reversing aspirin-induced intestinal lesions following the administration of a MAO inhibitor.

MPEP § 2163 states "An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formulas that fully set forth the claimed invention… one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable," 42 USPQ 2d 1001, Fed. Circuit (1997).

Example 5, pages 22-23, states

For the unmodified NSAIDS being given in combination with a MAO inhibitor, the MAO inhibitor was administered by oral gavage immediately prior to the administration of NSAID by oral gavage. Food was withheld tor 8 hours after the initial dosing. For acute studies, rats were euthanized by carbon dioxide, 8 hours after dosing and the stomachs were dissected. For modified NSAIDS with attached MAO inhibitors, the compounds were administered by oral gavage, food was withheld for 8 hours, animals were euthanized and the stomachs were examined tor the presence of lesions. For investigating the reversal of NSAID-induced gastric lesion, following 8 hours after NSAID dosing, the animals were provided food and water *ad libitum*. They were treated daily with oral gavage of MAO inhibitor for 7 days.

The NSAIDS produced significant gastrointestinal lesion (table 3). Pretreatment with 1-deprenyl provided protection against the NSAID induced gastric lesion. The NSAID attached to the MAO inhibitor also attenuated the gastric toxicity of NSAIDS. The gastric lesions were also reversed by daily administration of 1-deprenyl for 7 days.

There is no description directly relating to pretreatment that is supported by Table 3. Table 3 does not indicate there was any pretreatment of a MAO inhibitor. Table 3 also does not indicate there was reversal of existing gastrointestinal ulceration due to an anti-inflammatory drug. Table 3 merely shows a relative reduction of gastric lesions following aspirin ingestion when l-deprenyl is administered independently of aspirin, when aspirin is linked to propargylamine and when aspirin and l-deprenyl are administered for 7 days. Applicant has failed to provide a description drawn to a regimen to follow to reverse or to prevent ulceration following aspirin ingestion. No dosing regimens are described relating to dosing the claimed chemically linked, or "modified" aspirin-deprenyl, or, to independently dosing aspirin and propargylamine.

Table 3 does not support a pretreatment regimen. As such, Applicant was not in possession of the claimed subject matter at the time the invention was made.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai, C-S., U.S. Patent 5,916,910, in view of Xing et al., Digestive Diseases and Science.

Lai teaches the advantageous protective effects imparted by modifying a pharmacologically active agent, such as anti-inflammatory agent, into the form of a conjugate, to lower the incidence of side-effects. See the abstract. Specifically, Lai teaches the topical ulcerogenic effects of NSAIDS, as caused by aspirin, on the epithelium of the stomach, and the need to formulate modified dosage forms. See column 2, lines 53-59. Such conjugates can be covalently linked by amide linkages to reduce the side effects induced by aspirin, and, particularly, to reduce the topical irritant effect of aspirin. See column 22, lines 27-28. In Examples 5 and 6, columns 25-26, Lai evaluates the effects of a conjugate of gastric ulcers induced by a NSAID.

Although Lai's disclosure encompasses monoamine oxidase B inhibitors (column 10, line 20), of which deprenyl and propargylamine are examples, Lai fails to teach the

administration of a monoamine oxidase (MAO) B inhibitor to reduce the gastric ulcers that are the result of aspirin administration.

However, Xing teaches the selective MAO B inhibitors deprenyl and pargyline, a propargylamine derivative, attenuate gastric mucosal injury, gastric acid output and gastric mucosal blood flow. See the Abstract. Xing thus provides motivation to combine aspirin with a MAO B inhibitor.

Therefore, in view of the combined teachings of Lai and Xing, one skilled in the gastroenterology art would have been motivated to administer an anti-inflammatory agent such as aspirin, that is chemically linked, physically mixed or administered separately, with a MAO B inhibitor, with a reasonable expectation of reducing gastric ulceration. Such would have been obvious because the prior art recognized a need to modify ulcerogenic active agents by co-administering another agent that is effective in reducing the known gastric side-effect. In an animal model the claimed propargylamine derivatives clearly demonstrate efficacy in reducing the damage of gastric ulceration. Such reduction would reasonably enhance the beneficial anti-inflammatory effects of aspirin and provide gastric endothelial protection.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Jeff Lundgren, can be reached 571-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 2, 2011

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1629